

ABSTRACT

[0091] The present methods and apparatus 100 concern nucleic acid 214 sequencing by incorporation of nucleotides 218 into nucleic acid strands 220. The incorporation of nucleotides 218 is detected by changes in the mass and/or surface stress of the structure 116, 212. In some embodiments of the invention, the structure 116, 212 comprises one or more nanoscale or microscale cantilevers. In certain embodiments of the invention, each different type of nucleotide 218 is distinguishably labeled with a bulky group and each incorporated nucleotide 218 is identified by the changes in mass and/or surface stress of the structure 116, 212 upon incorporation of the nucleotide 218. In alternative embodiments of the invention only one type of nucleotide 218 is exposed at a time to the nucleic acids 214, 220. Changes in the properties of the structure 116, 212 may be detected by a variety of methods, such as piezoelectric detection, shifts in resonant frequency of the structure 116, 212, and/or position sensitive photodetection.